

Drug Shortages

Canadian Society of Hospital Pharmacist ON-Branch

2019

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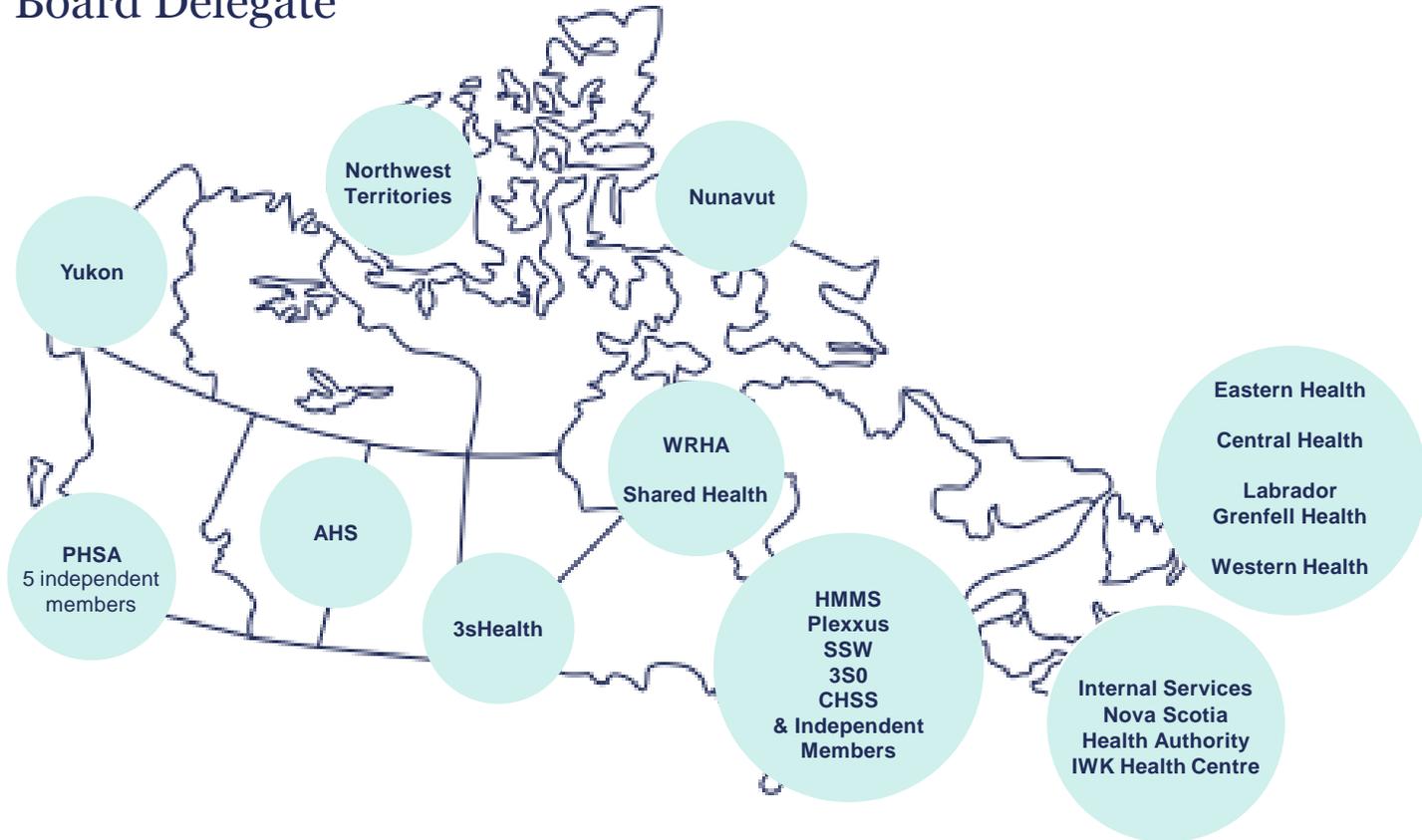


Veteran CSHP Member

Northern Chapter Chair

President Ontario Branch

Board Delegate



Disclosures

Clinical Director Pharmacy, HealthPRO

Member Support Newfoundland & Labrador

Drug Shortages

Oncology Contracting



Drug Shortage Story of Zinc

December 2012

Backorder of Zinc Sulfate 1 mg/mL

April 2013

Backorder resolved

186 neonatal & paediatric patients

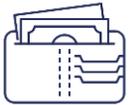
Learning Objectives



History of Drug Shortages in Canada



Impact of Drug Shortages on Patient Care



Drug Shortages a multi-stakeholder responsibility

- Overview of stakeholder involvement



Identify Strategies and Resources Pharmacists can Adopt in the Current Environment



Patient Care Impact

ISMP – Canada Survey

- 1 in 3 (35%) reported a near miss
- 1 in 4 reported actual error
- 1 in 5 reported an adverse patient outcome

Deaths & Critical Incidents

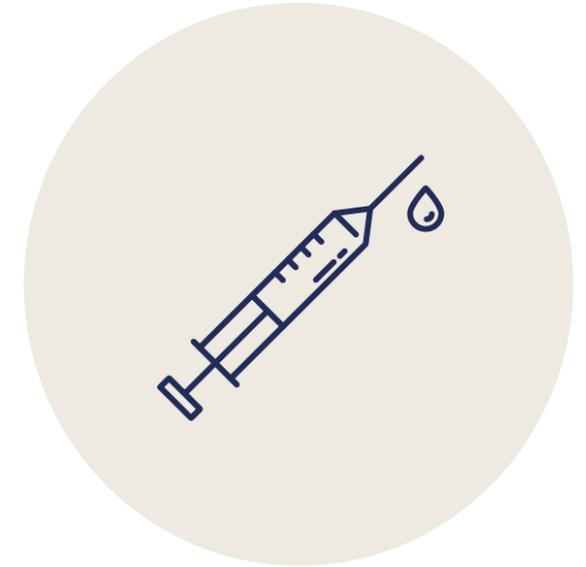
- HYDRomorphine at morphine dose

Diminished quality and accessibility of care

- (49%) respondents thought they had given an inferior anesthetic
- (13.9%) respondents regarded drug shortages as having prolonged recovery from anesthesia
- (7.8%) witnessing a drug error

Violation, delays, or compromised research protocols

Compounding – linked to sterility concerns and infection



Patient Care Impact

Compromise or Delay in Medical Treatment

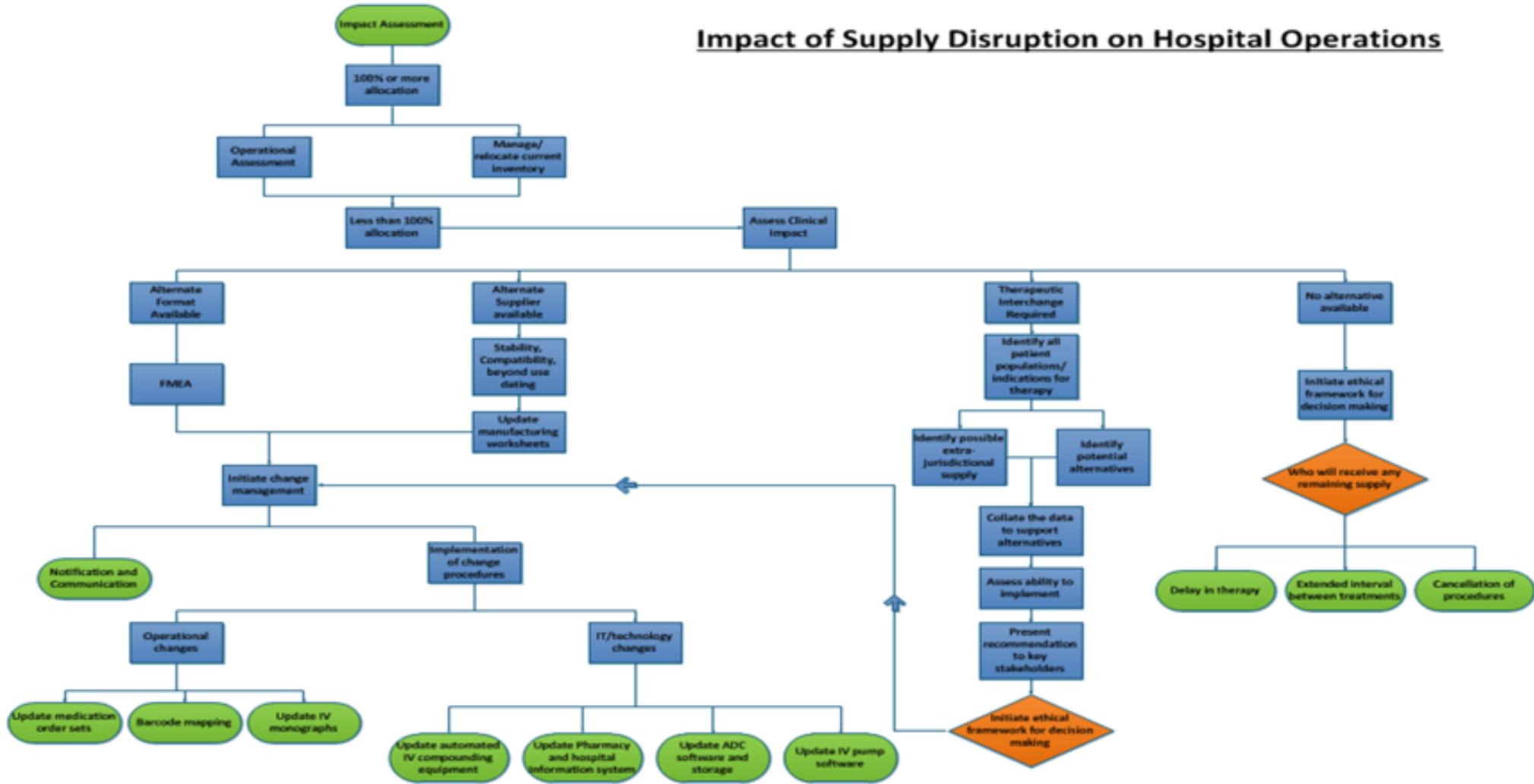
- Methylene blue: cancelled surgery
- Melphalan : BC delayed Bone Marrow transplant
- Etoposide: Denied Therapy
- BCG : Denied Therapy, rationed 1/3 of dose
- Vinorelbine : prioritization for curative intent

Hospitalization and Longer Hospital Stays

- Diminished effectiveness of alternate therapy
- Progression of disease
- Development of new health problems as a result of halted therapy of the drug in shortage



Impact of Supply Disruption on Hospital Operations





History of Drug Shortages

February 2012

November 2011 FDA warning

140 sole source injectable drugs

Entire injectable morphine family

March 2012

- CSHP & CPhA send a joint letter to federal Minister of Health
- HealthPRO, and GPOs write to Health Canada regarding shortages
- CSHP invited to speak House of Commons Standing Committee
- HealthPRO invited to speak House of Commons Standing Committee

June 2012

House of Commons Standing Committee on Health

- Issue a Report
- Drug Supply in Canada: A Multistakeholder Responsibility



Back it up: 2008

Baxter's heparin sodium MDV

350 Adverse Drug Reactions (ADR)
40% Serious ADRs
84 Deaths

Contaminated heparin

Changzhou SPL, China

Never inspected by China or FDA

2011

Health Canada warns of worsening drug shortages



Getty Images/Chris Hondros/Carly Weeks/Health Reporter/ published August 18, 2011



Are Shortages Improving?

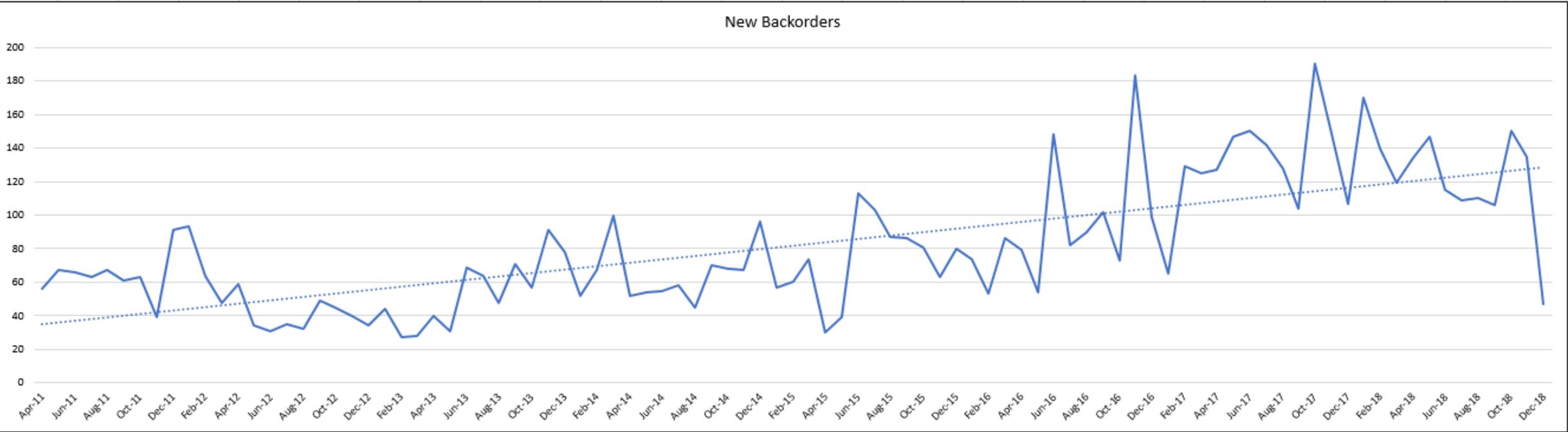
The Sandoz crisis was the worst shortages have ever been in Canada.

True

False

New Shortages April 2011 – December 2018

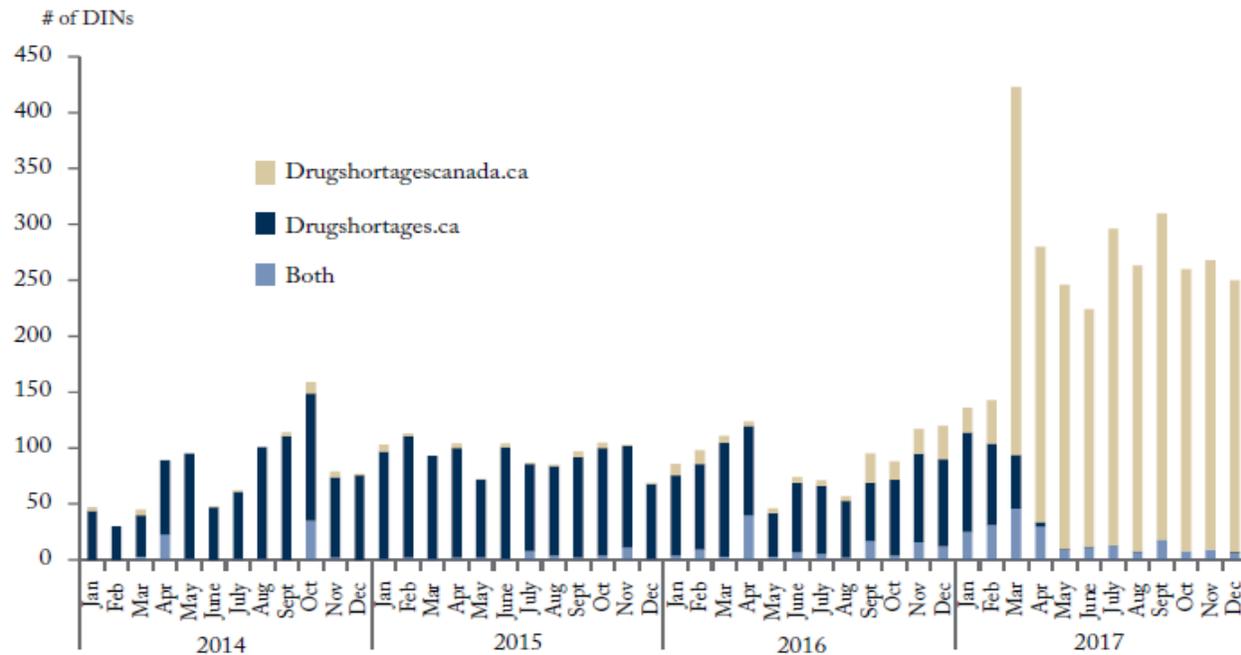
HealthPRO data:



New Shortages 2012-17

www.drugshortages.ca - www.drugshortagescanada.ca data

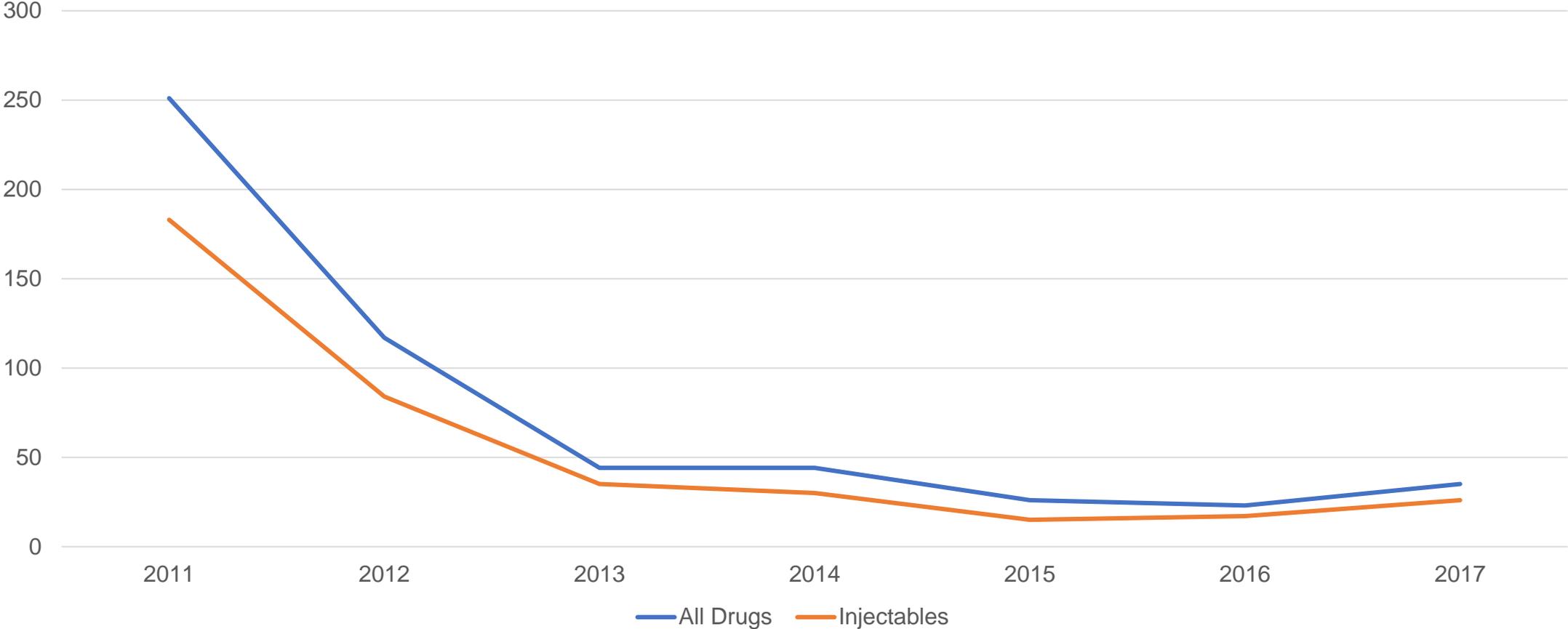
Figure 1: Drug Shortages per Month, Canada, 2012–17



Sources: www.drugshortages.ca, launched in 2012; and <https://www.drugshortagescanada.ca>, launched in March 2017.



FDA : 2011-17 Drug Shortages



<https://www.fda.gov/drugs/drug-shortages/drug-shortages-infographic>

2013- Canada's Journey of Shortages

Formation of MSCC on Drug Shortages

- Focus on prevention, notification, communication and mitigation of drug shortages

September 2013

- Toolkit for understanding Canada's drug shortages
- 11 problem areas identified classed into :
 - Drug Approvals
 - Manufacturing
 - Procurement and Distribution
 - Front Line Delivery

Front Line: Contribution to Problem

- **Inventory Management Strategies**

- Just in time – just in trouble

- **Stockpiling**

- Limits potential to re-allocate,
- Creates secondary shortages

- **Limited Drug Supply Movement**

- Limited movement between community and acute supply chain, and with health regions

Efforts implemented to address front line

MSSC Publication:

- Protocol for the Notification and Communication of Drug Shortages

Formation of the Provincial & Territories Drug Shortage Task Force

- **P/T Drug Task Force**

Formation of the Tier 3 Assessment Committee

- **TAC**

March 2019 – Formation of TAC

- Tier 3 Assignment Committee (TAC)
- The MSSC's Protocol for the Notification and Communication of Drug Shortages defines a Tier 3 shortage as a shortage with the greatest potential impact on Canadians where there are no available therapeutic alternatives marketed in Canada.
- TAC Membership

Tier 3 Assignment Committee Objectives

- Increase consistency and transparency in Tier 3 assignment
- Increase collaboration between stakeholders affected by drug shortages
- Contribute to effective case management of drug shortages

Procurement and Distribution : Drug Shortages

- **Sole Sourcing**

- Reliance on one manufacturer on behalf of many buyers
- Limits new market entrants
- Promotes market exit

- **Inventory Management at the Distributor**

- Minimal inventory results in ability to respond to increase in demand

Efforts Implemented to address contracting

MSSC Publication

- Guidance Document to Mitigate Drug Shortages Through Contracting and Procurement

Split Awards

- Award two suppliers
- 60/40 assignment

Alternate Supplier Awards

- Preferred alternate supplier

New Market Access Strategy

- Contract opportunity for new Canadian market entry

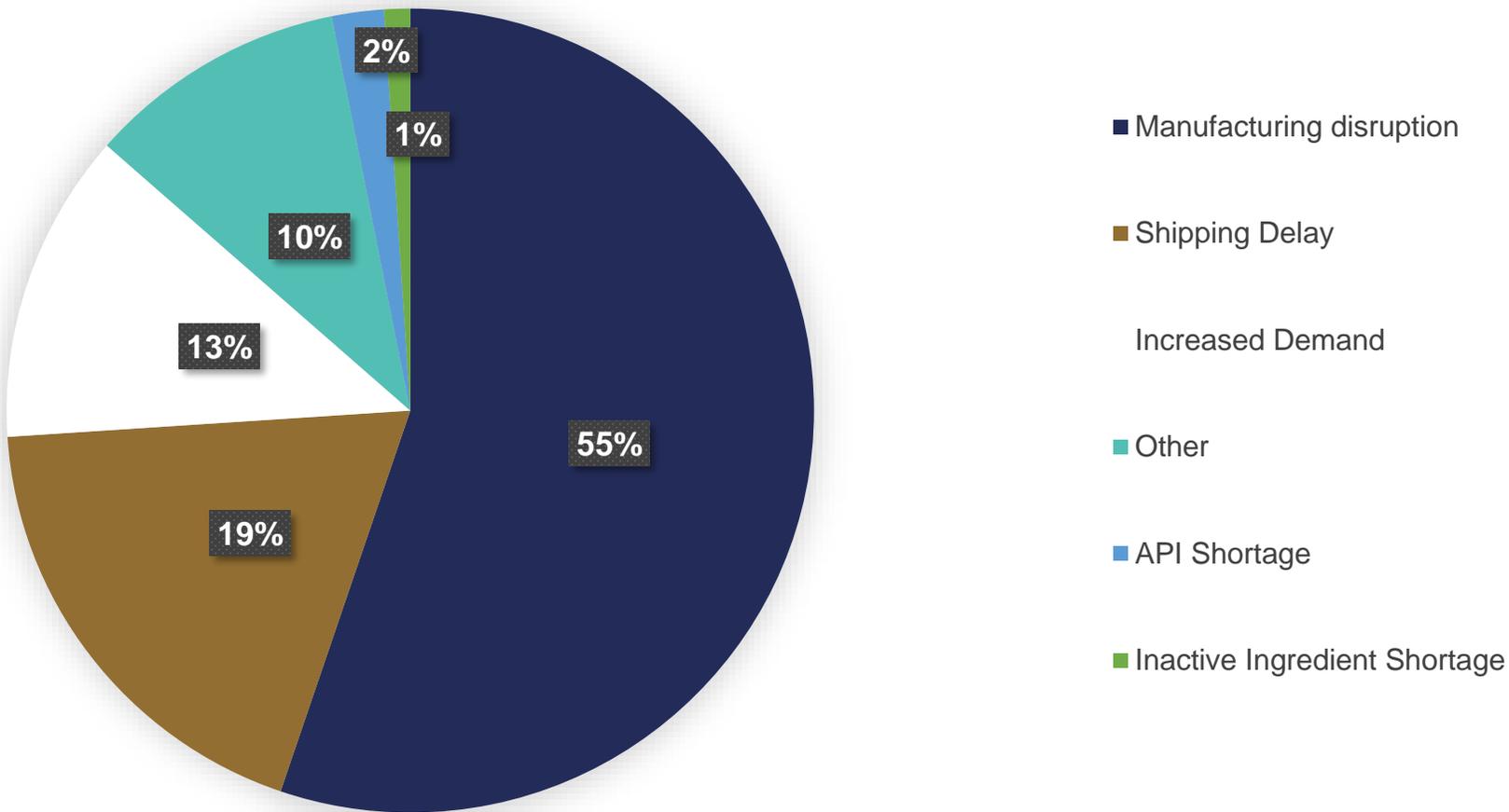
Reasons for Drug Shortages?

The most common reason for drug shortages is a global shortage of API.

True

False

All Shortages Reported : March 2017 to March 2019



Manufacturing: Contributing to the problem

- Non-compliance with standard manufacturing processes resulting in product recalls
- Non-compliance of foreign suppliers
- Single source foreign suppliers
- Changes in manufacturing procedures
- Global economic trends that lead to discontinuance of non-profitable products, downsizing product portfolios, and addition of new products that limits the capacity to manufacture existing products
- Unanticipated increases in demand
- Differing international regulatory requirements that make importing of foreign products during a shortage more challenging

ISPE – Drug Shortages Prevention Plan

- Corporate quality culture
- Robust quality system
- Metrics
- Business continuity planning,
- Communication with authorities
- Building capability.

<https://ispe.org/sites/default/files/initiatives/drug-shortages/drug-shortages-prevention-plan.pdf>

March 14, 2017

- 2015 Mandatory Reporting Announced
- Rona Ambrose- Health Minister
- Name and shame

2017

- Health Canada hosted website
- finally put into effect a mandatory reporting policy

Drug Shortages Defined

“Manufacturers will post all drug shortages, anticipated or actual as well as discontinuations, on drugshortages.ca, no less than six months in advance or if known less than six months in advance, it should be reported within five days from when they become aware of it, to allow maximum opportunity for the healthcare system to react to the shortage”

Drug shortages are really only a generic manufacturing company problem.

True

False

Shortages impact all drugs

Figure 9: Top 10 Drugs Producers by Number of Shortages, Canada, 2013–16

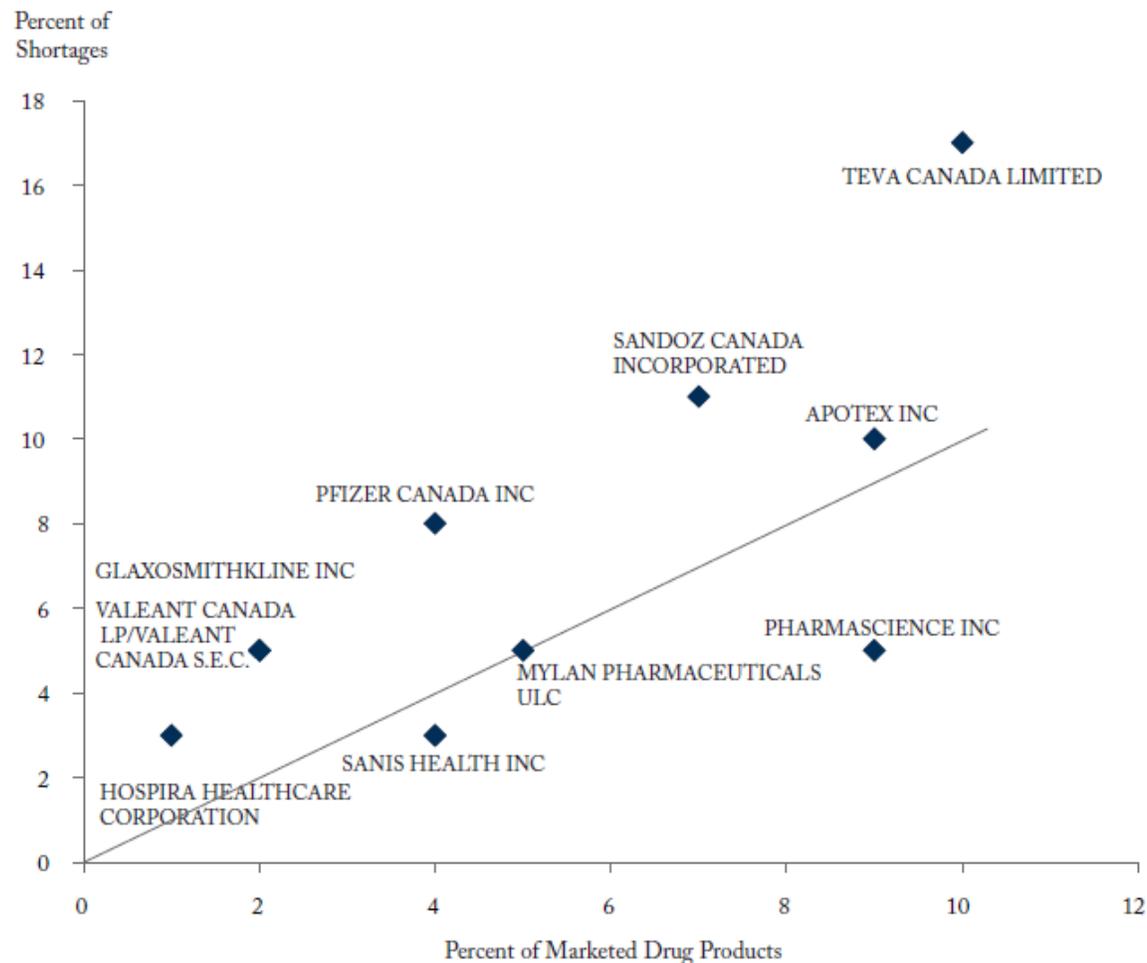
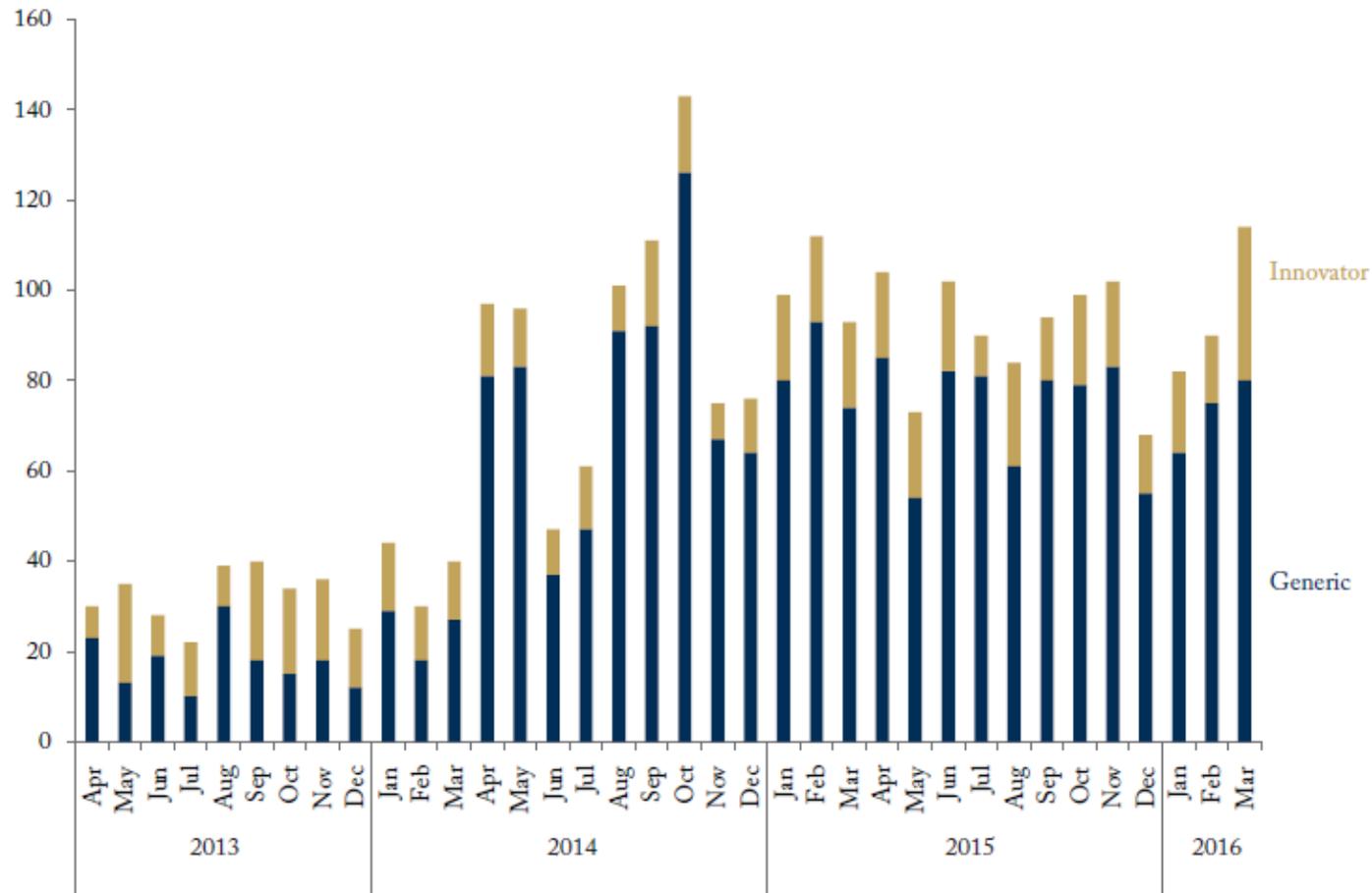


Figure 3: Shortages of Generic or Innovator Drug Products over a Three-Year Period, Canada, 2013–16



Note: Period covered is April 1, 2013–March 31, 2016.
 Source: www.drugshortages.ca, launched in 2012.

Shortages in Canada

Three-Year Period

- Generic drugs
- Innovator Drugs

https://www.cdhowe.org/sites/default/files/attachments/research_papers/mixed/Commentary_515.pdf

Regulatory Authorities – Part of the Problem & Solution

- GMP Inspections and Establishment License Actions
- Mutual Recognition Agreements
- Drug Approval Tools
- Expedited Lot Release

Multi-stakeholder – Health Canada

- Communication and Information Sharing : Multi-stakeholder calls
- Expedited Processing / Review of Submissions: Methylene Blue
- Expedited Lot Release: Calcitonin, Erwinase
- Special Access Program: Nimodipine
- Interim Order: Auvi-Q Epinephrine Auto-injectors
- Access to Drugs in Exceptional Circumstances: Naloxone Nasal Spray

Health Canada

- Work with Canadian Authorization holders
- The **Food and Drugs Act** and Regulations govern the importation and sale of drugs in Canada
 - Only compliant products permitted in Canada
- Enforcement discretion
 - No objection letters
 - Etoposide, Dexrazoxane, Succinylcholine, Fludarabine

Health Canada: Can't Do

Health Canada cannot require a pharmaceutical company to:

- Make a drug
- Make more of a drug
- Change how much and to whom the drug is distributed

Mitigation Strategies Beyond the Basics

- Multidisciplinary Communication
 - Regional
 - Provincial
 - National
- Explicit dose, therapeutic alternatives
- Forced Functions

Medication Posting

Important news and alerts about pharmacy products



Medication Posting

22 October 2018

Best Practice

Drug Discontinuation

Drug Shortage

Label/Packaging Change

Medication Change

Medication Safety

Recall

Vendor Change

For distribution by:

Pharmacy Managers/Directors

For the information of:

Pharmacy Staff
Patient Care Managers
Clinical Nurse Educators
Nursing Staff
Physicians

PLEASE POST

Update - Methylene Blue 10 mg/mL Injection - Shortage

The Issue:

Methylene blue 10 mg/mL, 1 mL and 5 mL injection are available in limited supply. Teligent brand is on a long-term back order due to a global Active Pharmaceutical Ingredient (API) shortage. Omega brand is currently available in extremely limited supply and is anticipated to be on back order sooner than originally expected; at the beginning of November 2018 (5 mL vial) and potentially by early December 2018 (1 mL vial) with no known release date.

Stock levels are critically low and will not meet current demands. Inventory will be depleted prior to the resolution of this back order.

Key changes include:

- Physicians should be aware of the shortage of methylene blue 10 mg/mL injection.
- To conserve our stock, reserve methylene blue injection for those patients with no other treatment options, including:
 - Symptomatic methemoglobinemia with concentrations > 20%
 - Iofamide-induced encephalopathy
 - Refractory hypotension (e.g., cardiac surgery, beta blocker/calcium channel blocker poisoning)
- Methylene blue 1% (10 mg/mL) and 2% (20 mg/mL) oral solution will be made available for chromoendoscopy*. Contact your site pharmacy to obtain supply.
- Oral phenazopyridine (compounded), intravenous fluorescein sodium, or bladder distention with sterile water or normal saline solution are alternative options to test ureter function at cystoscopy*
http://www.mdedge.com/sites/default/files/Document/September-2017/095_0914_EditorWEB.pdf
http://www.mdedge.com/sites/default/files/Document/January-2018/080MD100137_Evidence-PDF
- Patent blue sodium injection is an alternative lymphatic marker dye*.
- Patent blue sodium, fluorescein sodium, and indocyanine green (currently on back order) are the only alternative injectable sterile marker dyes available*; ensure appropriate dosing and indication. Patent blue and indocyanine green are obtained through CPISM.

*Alternatives are provided for clinician information and may not be appropriate for all clinical situations. The information provided does not replace clinician judgement.

Note: The Poison and Drug Information Service (PADIS) is available 24/7 by calling 1-800-332-1414 to assist with management of poisoning.

Action:

Please post this notice in your area and ensure all staff is informed about the change.

Contact Information:

Please contact your site pharmacy department with any questions or concerns.

Prepared by: Mandy De Jong, DUE Pharmacist, AHS Pharmacy Services

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MEDICATION ALERT

Important news and alerts about Pharmacy products.



Medication Alert

FEBRUARY 21, 2019

- Brand Change
- Drug Discontinuation
- Drug Shortage
- Formulary Addition
- Label Change
- Medication Change
- Recall

For the information of...

Pharmacy Staff
Patient Care Managers
Physicians
Nursing Staff

PLEASE POST

Medication Alerts are created expressly for use by Eastern Health and persons acting on behalf of Eastern Health for guidance and decisions made on behalf of Eastern Health. Any modification, use or adoption of this Medication Alert are done so at the risk of the adopting organization.

Methylene Blue – Drug Shortage Update

The Issue:

There is an ongoing national shortage of Methylene Blue 10 mg/mL injection. Omega Laboratories are the only current supplier to the Canadian market and their product has been on backorder since early December. Unfortunately the estimated end date of this backorder is unknown.

The current supply of Methylene Blue 10 mg/mL injection at Eastern Health facilities is extremely limited and we must now implement conservation measures to ensure product is available for those critical uses for which there are no alternatives.

Based on current known uses of Methylene Blue in Eastern Health and through consultation with Clinical departments it has been determined that Methylene Blue Injection should be reserved for:

- Symptomatic acquired Methemoglobinemia
- Refractory hypotension post cardiac surgery

To ensure that product remains available for these indications, the following steps will be taken:

- Methylene Blue injection will be removed from all wardstock/Pyxis areas not requiring it to treat these two conditions.
- Methylene Blue injection will be stocked in the Pyxis machines on the Cardio Critical Care Units in City Sites.
- A sufficient quantity of Methylene Blue injection required to treat Methemoglobinemia injection for one patient will be available in Pyxis Night Cupboards at Rural Sites.
- Pharmacy Services will obtain a supply of Patent Blue Injection as an alternative marker dye to be used instead of Methylene Blue where clinically appropriate.

Action:

Please post this notice in your area and ensure all staff is informed about this issue.

Contact:

Please contact Pharmacy Services at your site with any questions or concerns.



Methylene Blue Indication	Medically Necessary	Alternative(s) Identified	Available Alternatives	Potential Alternatives Identified not Marketed in Canada (SAP)	Stakeholders	Comments
Methemoglobinemia	Y	N	Oral methylene blue Supportive Care	Methylene blue (ProvayBlue)	PADIS Critical Care Emerg	Oral methylene blue undergoes substantial first pass metabolism so the effect may be slower than IV and may require repeated dosing q4h depending on what the drug/toxin is.
Ifosfamide induced encephalopathy	Y	N	Oral methylene blue Supportive Care	Methylene blue (ProvayBlue)	Oncology	Oral methylene blue not a good option due to low CNS penetration
Refractory hypotension (post cardiac surgery, BB/CCB overdose, shock)	Y	N	Supportive Care	Methylene blue (ProvayBlue)	PADIS Critical Care Emerg	Methylene blue is the last option for treatment
polypectomy/endoscopic tissue resections/ visualize precancerous cells (submucosal injection)	Y	N		Methylene blue (Eleview) Methylene blue (ProvayBlue) Methylene blue syringe (Macure Pharma) Indigocarmine	GI Endoscopy	?Patent blue The incidence of missing polypoid tissue during piecemeal is high and increased when the margins are not clear. The injectate allows us to establish a 'cushion' between the submucosa and the muscularis level and minimize damage to the muscularis during electrocautery
Ureter/bladder patency visualization during cystoscopy	N	Y	Oral phenazopyridine Intravenous flourescein Bladder distention (normal saline, sterile water, 10% dextrose)	Methylene blue (ProvayBlue) Methylene blue syringe (Macure Pharma) Indigocarmine	UroGyne	
Lymph node marking	N	Y	Patent blue	Methylene blue (ProvayBlue) Methylene blue syringe (Macure Pharma)	General Surgery	
Cataract surgery	N	Y	Fluorescein Indocyanine green	Methylene blue (ProvayBlue) Methylene blue syringe (Macure Pharma)	Ophth	

Prepared by Mandy De Jong, DUS Pharmacist, AHS November 26, 2018

Mitigation Strategies Beyond the Basics

- Identify critical medication list and assign therapeutic alternatives
 - HealthPRO commitment – Medically Necessary Hospital Drug List
- Form robust multi-disciplinary drug shortage teams
 - Pharmacy, Physicians, Nursing
 - Patient Advocates, Legal, and Ethical
- Pharmacist Prescribing
 - UK experience

Royal Pharmaceutical Society

Pharmacists able to prescribe independently, without consultation with the prescriber during a shortage.

- Reduce quantity
- Therapeutic equivalent
- Generic equivalent
- Alternative dosage form

Resources:

Websites:

- www.drugshortagescanada.ca
- www.medsask.usask.ca

- www.ashp.org
- www.fda.gov

Resources

Networks:

- HealthPRO
www.healthprocanada.com
- CSHP - QID
- CAPCA

Resources

Policies, Best Practices, & Guidelines

- MSSC Multi-Stakeholder Toolkit
- MSSC Protocol for the Notification and Communication of Drug Shortages
- Ethical Framework for Resource Allocation during Drug Shortages
- ISMP Drug Shortages and Medication Safety Concerns -2012
- CPhA Drug Shortages a Guide for Assessment and Patient Management

- ASHP Guidelines on Managing Drug Product Shortages
- Drug Product Shortages - ASHP Policy Position
- ASHP Guidance for Purchasing Drug Products in Short Supply
- A.S.P.E.N.'s Recommendations for Managing Parenteral Nutrition
- Sample Drug Shortages Policy by University Healthcare Hospitals and Clinics

Thank you.



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